

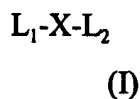
On page 95, the paragraph beginning on line 10:

A compound of formula (I) wherein L_1 comprises a nitrogen that is bonded to X, can be prepared by alkylating a corresponding compound of formula L_1-H wherein -H is bound to the nitrogen, with a corresponding compound of R_a-X-L_2 wherein X and L_2 have any of the values defined herein and R_a is a suitable leaving group. Suitable leaving groups [an] and conditions for the alkylation of an amine are known in the art (for example, see Advanced Organic Chemistry, Reaction Mechanisms and Structure, 4 ed., 1992, Jerry March, John Wiley & Sons, New York. For example, R_a can be halo (e.g. chloro, bromo, or iodo), methylsulfonyl, 4-tolylsulfonyl, mesyl, or trifluoromethylsulfonyl.

IN THE CLAIMS

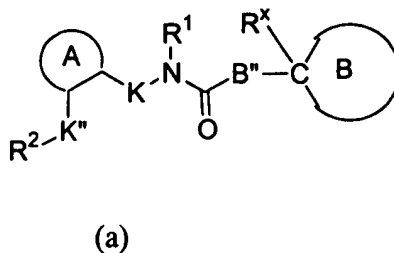
Please substitute the claim set in the appendix entitled Clean Version of Pending Claims for the previously pending claim set. The substitute claim set is intended to reflect amendment of previously pending claims 1, 2, 21-22, 26-27, 31, 33, 35, 39, 41, 49, 50 and 52. The specific amendments to individual claims are detailed in the following marked-up set of claims.

1. (Amended) A compound of Formula (I):



wherein:

L_1 is a group of formula (a):



wherein:

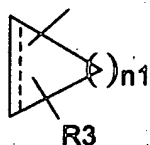
A is an aryl or a heteroaryl ring;

B" is -O-;

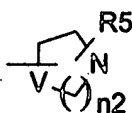
R^x is alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, acyl, acylamino, aminoacyloxy, aryl, carboxyalkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heteroaryl, heteroaralkyl, alkylsulfonyl, or alkylsulfinyl;

R¹ is hydrogen or alkyl;

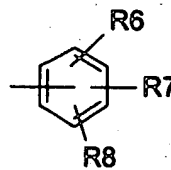
R² is Het, or is selected from a group consisting of formula (i), (ii), and (iii):



(i)



(ii)



(iii)

wherein:

----- is an optional double bond;

n₁ is an integer of from 1 to 4;

n₂ is an integer of from 1 to 3;

V is -CH-, -O-, -S(O)_{n₃}- (where n₃ is an integer of from 0 to 2), or -NR⁴- (wherein R⁴ is hydrogen, alkyl, substituted alkyl, aryl, or heteroaryl);

"Het" is a heteroaryl ring which optionally attaches (a) to a linker;

R³ is hydrogen, alkyl, halo, amino, substituted amino, -OR^a (where R^a is hydrogen, alkyl, or acyl), or a covalent bond attaching (a) to a linker;

R⁵ is hydrogen, alkyl, halo, amino, substituted amino, -OR^b (where R^b is hydrogen or alkyl), aryl, aralkyl, heteroaralkyl, or a covalent bond attaching (a) to a linker;

R⁶, R⁷, and R⁸ are, independently of each other, hydrogen, halo, hydroxy, alkoxy, haloalkoxy, carboxy, alkoxycarbonyl, alkyl optionally substituted with one, two or three substituents selected from halo, hydroxy, carboxy, alkoxycarbonyl, alkylthio, alkylsulfonyl, amino, substituted amino, or a covalent bond attaching (a) to a linker;

K is a bond or an alkylene group;

K" is a bond, -C(O)-, -S(O)_{n4}- (where n₄ is an integer of from 0 to 2), or an alkylene group optionally substituted with a hydroxyl group; and

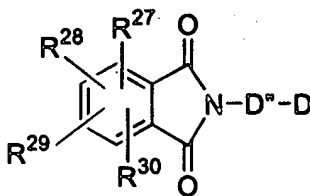
B is heterocycloamino or heteroaryl amino, which optionally attaches (a) to a linker; provided that at least one of the R³, R⁵, R⁶, R⁷, R⁸, "Het", heterocycloamino, or heteroaryl amino groups attaches (a) to a linker;

X is a linker; and

L₂ is an organic group comprising at least one primary, secondary or tertiary amine; or a pharmaceutically acceptable salt; or prodrug thereof.

2. (Amended) The compound of claim 1 wherein L₂ is a group selected from a group consisting of:

(i) a group of formula (b):



(b)

wherein:

D'' is alkylene;

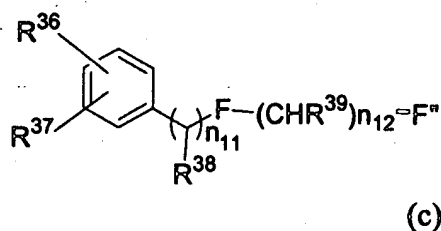
D is -NR³¹R³², -N⁺(R³³R³⁴R³⁵) or -OR³² where R³¹, R³³, and R³⁴ are, independently of each other, hydrogen, alkyl, or aralkyl; and R³² and R³⁵ represent a covalent bond attaching (b) to a linker;

R²⁷ is hydrogen, halo, nitro, cyano, hydroxy, alkoxy, carboxy, alkoxycarbonyl, acyl, thio, alkylthio, alkylsulfonyl, alkylsulfinyl, sulfonamido, alkylsulfonamido, carbamoyl, thiocarbamoyl, mono or dialkylcarbamoyl, amino, mono- or dialkylamino, aryl, aryloxy, arylthio, heteroaryl, heteraryloxy, heteroarylthio, heterocyclyl, heterocyclyloxy, aralkyl, heteroaralkyl, or alkyl optionally substituted with one, two or three substituents selected from halo, hydroxy, carboxy, alkoxycarbonyl, alkylthio, alkylsulfonyl, amino, or substituted amino;

R^{28} is hydrogen, halo, nitro, cyano, hydroxy, alkoxy, carboxy, alkoxy carbonyl, acyl, thio, alkylthio, alkylsulfonyl, alkylsulfinyl, sulfonamido, alkylsulfonamido, carbamoyl, thiocarbamoyl, mono or dialkylcarbamoyl, amino, mono- or dialkylamino, or alkyl optionally substituted with one, two, or three substituents selected from halo, hydroxy, carboxy, alkoxy carbonyl, alkylthio, alkylsulfonyl, amino, or substituted amino;

R^{29} and R^{30} are, independently of each other, hydrogen, alkyl, haloalkyl, halo, nitro, cyano, hydroxy, alkoxy, alkoxy carbonyl, acyl, thio, alkylthio, amino, mono- or dialkylamino; or one of R^{27} , R^{28} , R^{29} , or R^{30} together with the adjacent group forms a methylenedioxy or ethylenedioxy group;

(ii) a group of formula (c):



wherein:

n_{11} is an integer of from 1 to 7;

n_{12} is 0 to 7;

F is $-NR^{40}-$, $-O-$, $-S-$, or $-CHR^{41}-$ (wherein R^{40} and R^{41} are, independently of each other, hydrogen, alkyl, or substituted alkyl);

F' is a covalent bond, $-OR^{43}$, $-NR^{42}R^{43}$, or $-N^+R^{43}R^{44}R^{45}$ wherein R^{42} is hydrogen or alkyl, R^{44} and R^{45} are alkyl, and R^{43} is hydrogen, alkyl, or a covalent bond attaching (c) to a linker;

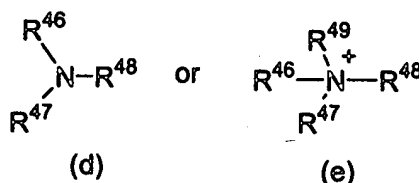
R^{36} is hydrogen, alkyl, halo, nitro, cyano, hydroxy, alkoxy, carboxy, alkoxy carbonyl, acyl, thio, alkylthio, alkylsulfonyl, alkylsulfinyl, sulfonamido, alkylsulfonamido, carbamoyl, thiocarbamoyl, mono or dialkylcarbamoyl, amino, mono- or dialkylamino, aryl, aryloxy, arylthio, heteroaryl, heteraryloxy, heteroarylthio, heterocyclyl, heterocyclyloxy, aralkyl, heteroaralkyl, or alkyl optionally substituted with one, two or three substituents selected from halo, hydroxy, carboxy, alkoxy carbonyl, alkylthio, alkylsulfonyl, amino, or substituted amino;

R³⁷ is hydrogen, alkyl, halo, nitro, cyano, hydroxy, alkoxy, alkoxycarbonyl, acyl, thio, alkylthio, amino, mono- or dialkylamino, aryl, aryloxy, arylthio, heteroaryl, heteraryloxy, heteroarylthio, heterocyclyl, heterocyclyloxy, aralkyl, heteroaralkyl, or alkyl optionally substituted with one, two or three substituents selected from halo, hydroxy, carboxy, alkoxycarbonyl, alkylthio, alkylsulfonyl, amino, or substituted amino; and

R³⁸ is hydrogen, alkyl, halo, hydroxy, alkoxy, or a covalent bond attaching the ligand to a linker provided that at least one of R³⁸ and R⁴³ attaches (c) to a linker;

R³⁹ is hydrogen, alkyl, halo, hydroxy, alkoxy, or substituted alkyl; and

(iii) a group of formula (d) or (e):



wherein:

R⁴⁶ is alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, or heterocycle;

R⁴⁷ is alkyl, substituted alkyl, aryl, acyl, heterocycle, or -COOR⁵⁰ where R⁵⁰ is alkyl; or

R⁴⁶ and R⁴⁷ together with the nitrogen atom to which they are attached form a heterocycle, which heterocycle[, in addition to optionally bearing the optional substituents defined hereinbelow for a heterocycle, can also] is optionally [be] substituted with one or more [(e.g. 1, 2, 3, or 4)] alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, [or] substituted alkynyl, alkoxy, substituted alkoxy, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, acyl, acylamino, acyloxy, amino, substituted amino, aminoacyl, aminoacyloxy, oxyaminoacyl, azido, cyano, halogen, hydroxyl, keto, thioketo, carboxyl, carboxylalkyl, thioaryloxy, thioheteroaryloxy, thioheterocycloxy, thiol, thioalkoxy, substituted thioalkoxy, aryl, aryloxy, heteroaryl, heteroaryloxy, heterocyclic, heterocycloxy, hydroxyamino, alkoxyamino, nitro, -SO-alkyl, -SO-substituted alkyl, -SO-aryl, -SO-heteroaryl, -SO₂-alkyl, -SO₂-substituted alkyl, -SO₂-aryl or -SO₂-heteroaryl[.];

R⁴⁸ is a covalent bond that attaches the (d) to a linker; and

R⁴⁹ is alkyl;

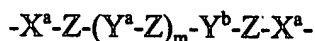
or a pharmaceutically acceptable salt; or prodrug thereof.

21. (Amended) The compound of claim 20 wherein: R⁴⁶ is alkyl or substituted alkyl; R⁴⁷ is alkyl, substituted alkyl, or heterocycle; or R⁴⁶ and R⁴⁷ together with the nitrogen atom to which they are attached form a heterocycle.

22. (Amended) The compound of claim 1 or 2 wherein L₂ has any one of the formulas A1-A590 [shown hereinabove] in Table 1.

26. (Amended) The compound of claim 1 or 2 wherein X is alkylene optionally substituted with one, two, or three hydroxy groups, alkylene wherein one, two, or three carbon atoms have been replaced by an oxygen atom, or an -alkylene-phenylene-alkylene- wherein the phenylene ring is optionally substituted with one or two chloro or fluoro groups.

27. (Amended) The compound of claim 1 or 2 wherein X is a group of formula:



wherein

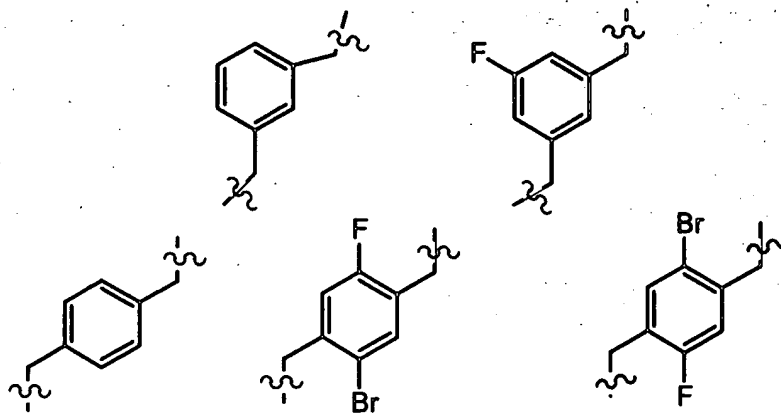
m is an integer of from 0 to 20;

X^a at each separate occurrence is selected from the group consisting of -O-, -S-, -NR-, -C(O)-, -C(O)O-, -C(O)NR-, -C(S)-, -C(S)O-, -C(S)NR- or a covalent bond where R is as defined below;

Z at each separate occurrence is selected from the group consisting of alkylene, substituted alkylene, cycloalkylene, substituted [cylcoalkylene,] cycloalkylene, alkenylene, substituted alkenylene, alkynylene, substituted alkynylene, cycloalkenylene, substituted cycloalkenylene, arylene, heteroarylene, heterocyclene, [or] and a covalent bond;

Y^a and Y^b at each separate occurrence are selected from the group consisting of -O-, -C(O)-, -OC(O)-, -C(O)O-, -NR-, -S(O) $_n$ -, -C(O)NR'-, -NR' C(O)-, -NR' C(O)NR'-, -NR' C(S)NR'-, -C(=NR')-NR'-, -NR'-C(=NR')-, -OC(O)-NR'-, -NR'-C(O)-O-, -N=C(X^a)-NR'-, -NR'-C(X^a)=N-, -P(O)(OR')-O-, -O-P(O)(OR')-, -S(O) $_n$ CR'R''-, -S(O) $_n$ -NR'-, -NR'-S(O) $_n$ -, -S-S-, and a covalent bond; where n is 0, 1 or 2; and R, R' and R'' at each separate occurrence are selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkenyl, substituted alkenyl, cycloalkenyl, substituted cycloalkenyl, alkynyl, substituted alkynyl, aryl, heteroaryl and heterocyclic; provided at least one of X^a, Y^a, Y^b or Z is not a covalent bond.

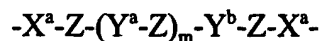
31. (Amended) The compound of claim 1 or 2 wherein X has one of the following [the] formulas:



or a pharmaceutically acceptable salt or prodrug thereof.

33. (Amended) The compound of claim 1 or 2 wherein L₂ is a group of formula A234, A363, A364, A153, A28, A324, A329, A562, A87, or A239 [as described herein] in Table 1.

35. (Amended) The compound of claim 34 wherein X is a group of formula:



wherein

m is an integer of from 0 to 20;

X^a at each separate occurrence is selected from the group consisting of -O-, -S-, -NR-, -C(O)-, -C(O)O-, -C(O)NR-, -C(S)-, -C(S)O-, -C(S)NR-, or a covalent bond [where R is as defined below];

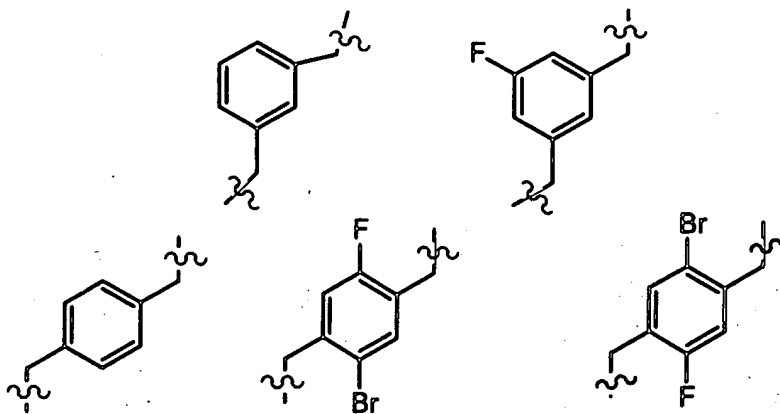
Z at each separate occurrence is selected from the group consisting of alkylene, substituted alkylene, cycloalkylene, substituted [cylcoalkylene,] cycloalkylene, alkenylene, substituted alkenylene, alkynylene, substituted alkynylene, cycloalkenylene, substituted cycloalkenylene, arylene, heteroarylene, heterocyclene, or a covalent bond;

Y^a and Y^b at each separate occurrence are selected from the group consisting of -O-, -C(O)-, -OC(O)-, -C(O)O-, -NR-, -S(O) n -, -C(O)NR'-, -NR' C(O)-, -NR' C(O)NR'-, -NR' C(S)NR'-, -C(=NR')-NR'-, -NR'-C(=NR')-, -OC(O)-NR'-, -NR'-C(O)-O-, -N=C(X^a)-NR'-, -NR'-C(X^a)=N-, -P(O)(OR')-O-, -O-P(O)(OR')-, -S(O) n CR'R''-, -S(O) n -NR'-, -NR'-S(O) n -, -S-S-, and a covalent bond;

[where] n is 0, 1 or 2; and

R, R' and R'' at each separate occurrence are selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkenyl, substituted alkenyl, cycloalkenyl, substituted cycloalkenyl, alkynyl, substituted alkynyl, aryl, heteroaryl and heterocyclic; provided at least one of X^a , Y^a , Y^b or Z is not a covalent bond.

39. (Amended) The compound of claim 34 wherein X has one of the following [the] formulas:



41. (Amended) The compound of claim 2 wherein [wherein] L_2 is a group of formula (d) wherein R^{46} is alkyl that is optionally substituted with from 1 to 5 substituents independently selected from the group consisting of alkoxy, substituted alkoxy, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, acyl, acylamino, acyloxy, amino, aminoacyl, aminoacyloxy, oxyaminoacyl, cyano, halogen, hydroxyl, keto, thioketo, carboxylalkyl, thioaryloxy, thioheteroaryloxy, thioheterocycloxy, thiol, thioalkoxy, substituted thioalkoxy, heterocyclic, heterocycloxy, hydroxyamino, alkoxyamino, and NR^aR^b , wherein R^a and R^b may be the same or different [and] and are chosen from hydrogen, alkyl, substituted alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, and heterocyclic.

49. (Amended) The method of claim 48 wherein the disease is urinary incontinence, chronic pulmonary obstructive disease, asthma, hyper salivation, a cognitive disorder, blurred vision, or irritable bowel syndrome.

50. (Amended) A compound of formula L_1-H wherein L_1 [,] has the values defined in claim 1; or a salt thereof.

52. (Amended) A compound of formula R_a-X-L_2 wherein X [,] and L_2 have the values defined